UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte WILLIAM S. M. WOLD, KAROLY TOTH, KONSTANTIN DORONIN and ANN E. TOLLEFSON

Appeal No. 2005-1444
Application No. 09/351,778

ON BRIEF

Before ELLIS, ADAMS, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 11-15, 20-22, 24, 32-44, 60-75 and 97-108.[1] Claims 13, 60 and 102 are representative of the subject matter on appeal, and read as follows:

[1] Claims 1-4, 10, 45-59 and 85-96 have been cancelled, claims 6-9, 16-19, 23, 25-31 and 76-84 have been withdrawn from consideration as being drawn to a non-elected invention, and claim 5 has been indicated as being allowable. See Examiner's Answer, page 2. Claim 5 is drawn to "[a] recombinant adenovirus that comprises SEQ ID NO:1 or SEQ ID NO:2."

13. A method for treating cancer in an animal having a tumor comprising administering to the tumor an adenovirus vector wherein said adenovirus vector is replication-competent in neoplastic cells and overexpresses an adenovirus death protein (ADP), wherein overexpression is defined as overexpression relative to *dl*309.

60. A method for treating cancer in an animal having a tumor, the method comprising administering to the tumor an adenovirus vector that is replication-competent in neoplastic cells and expresses an adenovirus death protein (ADP), wherein:

a) the ADP is expressed from an ADP coding sequence positioned under the control of a promoter other than the endogenous promoter for ADP;

b) the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA;

c) the ADP is expressed from an ADP coding sequence flanked by a pre-mRNA splicing and cleavage/polyadenylation signal other than the pre-mRNA splicing and cleavage/polyadenylation signal normally associated with the ADP gene, and/or

d) the ADP is expressed from an ADP coding sequence that is positioned downstream of the coding sequence for another adenovirus mRNA, together with a sequence on the 5' side of the ADP coding sequence that allows for internal initiation of translation of ADP.

102. A method for treating cancer in an animal having a tumor, the method comprising administering to the tumor an adenovirus vector wherein said adenovirus vector is replication competent in neoplastic cells and overexpreses an adenovirus death protein (ADP), wherein overexpression is effected by one or more of the following modifications:

a) the ADP is expressed from an ADP coding sequence positioned under the control of a promoter other than the endogenous promoters for ADP;

b) the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA;

c) the ADP is expressed from an ADP coding sequence flanked by a pre-mRNA splicing and cleavage/polyadenylation signal other than the pre-mRNA splicing and cleavage/polyadenylation signal normally associated with the ADP gene, and/or

d) the ADP is expressed from an ADP coding sequence that is positioned downstream of the coding sequence for another adenovirus mRNA, together with a sequence on the 5' side of the ADP coding sequence that allows for internal initiation of translation of ADP.

Claims 11-15, 20-22, 24, 32-44, 60-75 and 97-108 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description

requirement, i.e., new matter. In addition, claims 101 and 102 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. And finally, claims 11-13, 32-44, 60, 61, 68, 69, 72-75, 97-99 and 101-108 stand rejected under 35 U.S.C. §102(e) as being anticipated by either Henderson[2] or Little,[3] and claims 13, 20-22, 60 and 64-66 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Henderson or Little as combined with Freytag.[4] After careful review of the record and consideration of the issues before us, we reverse the rejections under 35 U.S.C. § 112, first paragraph, except as to claims 32 and 104-106, which rejection is affirmed. We affirm the rejections under 35 U.S.C. § 112, second paragraph, 35 U.S.C. § 102(e) and 35 U.S.C. § 103(a).

BACKGROUND

"Cancer is a leading cause of death in the United States and elsewhere." Specification, page 1. According to the specification, "[n]ew therapies are necessary, to be used alone or in combination with classical techniques," and that "[o]ne potential therapy under active investigation is treating tumors with recombinant viral vectors expressing anti-cancer therapeutic proteins." Id. at 1-2.

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[2] Henderson et al. (Henderson), U.S. Patent No. 6,197,293, issued March 6, 2001, filed March 2, 1998.
[3] Little et al. (Little), U.S. Patent No. 6,254,862, issued July 3, 2001, filed March 2, 1998.
[4] Freytag et al. (Freytag), "A Novel Three-Pronged Approach to Kill Cancer Cells Selectively: Concomitant Viral, Double Suicide Gene, and Radiotherapy," Human Gene Therapy, Vol. 9, pp. 1323-33 (1998).

The specification teaches that:

> [T]he present invention is directed to novel vectors which are replication competent in neoplastic cells and which overexpress an adenovirus death protein (ADP). The work reported herein demonstrates the discovery that overexpression of ADP by a recombinant adenovirus allows the construction of a replication-competent adenovirus that kills neoplastic cells and spreads from cell-to-cell at a rate similar to or faster than that exhibited by adenoviruses expressing wild-type levels of ADP, even when the recombinant adenovirus contains a mutation that would otherwise reduce its replication rate in non-neoplastic cells. This discovery was unexpected because it could not have been predicted from what was known about adenovirus biology that Ad vectors overexpressing ADP remain viable and that the infected cells are not killed by the higher amounts of ADP before the Ad vector produces new virus particles that can spread to other tumor cells. Indeed, naturally-occurring adenoviruses express ADP in low amounts from the E3 promoter at early stages of infection, and begin to make ADP in large amounts only at 24-30 [hours post-infection], once virions have been assembled in the cell nucleus. It is believed that other non-adenoviral vectors can be used to deliver ADP's cell-killing activity to neoplastic cells, including other viral vectors and plasmid expression vectors.
>
> Thus, in one preferred embodiment, the ADP-expressing vector comprises a recombinant adenovirus lacking expression of at least one E3 protein selected from the group consisting of: gp19K; RIDα (also known as 10.4K); RIDβ (also known as 14.5K) and 14.7K. Because these E3 proteins inhibit immune-mediated inflammation and/or apoptosis of Ad-infected cells, it is believed that a recombinant adenovirus lacking one or more of these E3 proteins will stimulate infiltration of inflammatory and immune cells into a tumor treated with the adenovirus and that this host immune response will aid in destruction of the tumor as well as tumors that have metastasized. The ADP expressed by preferred embodiments comprises a naturally-occurring amino acid sequence from a human adenovirus of subgroup C, namely Ad1, Ad2, Ad5 and Ad6.

Id. at 5-6.

DISCUSSION

1. Rejection under 35 U.S.C. § 112, first paragraph

Claims 11-15, 20-22, 24, 32-44, 60-75 and 97-108 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The burden is on the examiner to set forth a prima facie case of unpatentability. See In re Alton, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1581 (Fed. Cir. 1996). The disclosure as originally filed need not provide "in haec verba support for the claimed subject matter at issue," rather, the disclosure should convey to one skilled in the art that the inventor was had possession of the invention at the time of filing. Purdue Pharma L.P. v. Faulding Pharmaceutical Co., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) (citations omitted).

Claims 13, 60, 101 and 102, and the claims dependent thereon, stand rejected for reciting "method for treating cancer in an animal having a tumor." Examiner's Answer, page 4. The examiner notes that appellants have not indicated where support may be found for the objected to language. Moreover, according to the examiner, "[a]nimals include organisms from protozoans to sponges and on up to mammals," and that the specification refers to treating

cancer in patients, which, when read in light of page 1, line 10 of the specification, refers to humans. Id. at 4-5.

Appellants argue, citing page 17, lines 16-21 of the specification, that the specification contemplates the treatment of "'tumors of any origin.'" Appeal Brief,[5] pages 6-7. Moreover, appellants contend, Examples 4 and 8 of the specification demonstrate the treatment of mice having tumors, and specifically use the word animal at page 27 of the specification, lines 20-21. See id. at 7. Finally, appellants assert, the term patient encompasses animal patients as well as human patients. See id.

We agree with appellants that the specification, as discussed above, provides support for a "method for treating cancer in an animal having a tumor," and the rejection is reversed. We find that the discussion of treatment of tumors of any origin, as well as the examples, would convey to the skilled artisan that the inventors had possession of the claimed invention at the time of filing.

Claim 13 and the claims dependent thereon stand rejected for reciting that overexpression of ADP is defined by overexpression of ADP by the adenovirus vector relative to *dl*309. See Examiner's Answer, page 5. The Examiner asserts that *dl*309 is not wild-type adenovirus, and that the examples relied upon to support the limitation refer only "to the KD and GZ vectors, and

[5] All references to the "Appeal Brief" in this opinion refer to the "Supplemental Brief on Appeal," dated November 18, 2004.

does not describe such a comparison as being generally determinative of an adenovirus vector overexpressing ADP." Id. at 5-6.

Appellants first point out that the specification at page 25, lines 28-30, "characterizes Ad5, *dl*309 and *dl*01/07 as 'viruses expressing wild-type amounts of ADP.'" Appeal Brief, page 8. Moreover, assert appellants, the specification makes clear that "the inventors contemplated that *dl*309 was intended to be a standard against which one can measure overexpression." Id. Again, we agree with appellants for the reasons stated, and the rejection is reversed.

Claim 32 stands rejected for reciting "that ADP overexpression 'is detectable by western blot, cell lysis, virus release, or by cell spreading assay.'" Examiner's Answer, page 6. Claims 103-106 stand rejected for reciting each of those assays individually. See id. The examiner asserts that "Example 2 does not teach that any of these methods are to be used to determine whether ADP is overexpressed. Instead, these assays were used to characterize KD1 and KD3 infection, and the consequence of ADP overexpression." Id. The examiner concludes that "[w]hile ADP overexpression may lead to increased rate of cell lysis, virus release or cell spread, it does not follow that an increased rate of cell lysis or cell spread displayed by an adenovirus vector, whose level of ADP expression is unknown, means the adenovirus vector overexpresses ADP, as is implied by the claim limitations." Id.

Appellants argue that the issue "is the 'overexpressing' language and how to interpret that language." Appeal Brief, page 11. Appellants contend that the

specification makes clear that overexpression of ADP is a central focus of the invention, and that Example 1 provides four examples of how to measure overexpression, and "in no way implies that these four methods are only applicable to KD1, KD2, GZ1 and GZ3 – on the contrary, the specification nowhere says that ADP overexpression is only desirable for these four vectors, and the examples merely provide an example as to how one might proceed to measure ADP expression." Id.

We agree with the examiner as to cell lysis, virus release and cell spreading assays, and the rejection is affirmed except as to claim 103. In Example 1, ADP expression is analyzed by immunoblot. See Specification, page 24, lines 11-27. Once ADP expression was determined, Example 2 looked at the consequences of that over expression, such as cell lysis, virus release and cell-spreading. See id. at 25, Example 2. There is no statement that these methods are directly correlated to ADP expression as measured by immunoblot, and thus, these examples would not convey to the skilled artisan that appellants had possession of the invention as now claimed.

Claim 60 and the claims dependent thereon stand rejected for reciting a series of four structural features, (a)-(d) characterizing the adenovirus vector, specifically, for reciting a) ... ; b)....; c) ..., and/or d).... See Examiner's Answer, page 7. The examiner contends that the disclosure as filed "presents these four characteristics as alternatives for achieving ADP overexpression," and "[i]t does

not teach or even imply including more than one of these alternatives within a single adenovirus vector." Id.

Appellants assert that page 13, lines 2-8, particularly at line 5, the specification, that although "this excerpt presents these four characteristics as alternatives," "it also presents these characteristics as cumulative and combinable, particularly in light of the fact that the specification specifically employs the inclusive connector 'and' when listing the possible elements." Appeal Brief, page 12. Again, we agree with appellants, and the rejection is reversed.

2. Rejection under 35 U.S.C. § 112, second paragraph

Claims 101 and 102 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that appellant regards as the invention.

Claims 101 and 102, according to the examiner, are indefinite in reciting "overexpresses an adenoviral death protein," as that recitation "renders these claims unclear as to the meets and bounds of the adenoviral vector." Examiner's Answer, page 7. According to the examiner:

> It is unclear in what context "overexpresses" is directed or applied to (i.e. overexpresses relative to what?). Wild-type adenoviruses typically "overexpress" ADP at very late stages of the infection cycle. Thus, a reasonably broad interpretation of these claims would suggest any adenovirus carrying ADP operably linked to its native promoters, and subject to natural expression control would inherently meet the limitation of the claims as written.

Id. at 7-8.

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." Miles Laboratories, Inc. v. Shandon, Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). Claims are in compliance with 35 U.S.C. § 112, second paragraph, if "the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits." Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1987). We agree with the reasons set forth by the examiner that the use of "overexpresses" renders the claims indefinite, and the rejection is affirmed.

Appellants contend

> that there is a specific definition, at page 12, lines 18-23, for what overexpression is measured against in the context of claims such as claims 101-102 that do not specify the reference virus. Here it is stated that "'overexpresses ADP' means that more ADP molecules are made per viral genome present in a dividing cell infected by the vector than expressed by any previously known recombinant adenoviral vector or AAV in a dividing cell of the same type."

Appeal Brief, page 12. According to appellants, "an adenovirus would only meet the limitation of the claims if it was shown to express more ADP molecules per viral genome present in a dividing cell infected by the vector than expressed by any previously known recombinant adenoviral vector in a dividing cell of the same type." Id. at 13.

However, it is the comparison to "any previously known recombinant adenoviral vector," which is how "overexpression" is defined in the specification,

that renders the claims indefinite. It is unclear what is encompassed by "any previously known recombinant adenoviral vector," in that does "known" encompass only recombinant adenoviruses that were published before the filing date of the application, recombinant adenoviruses that were made but not published, or does it encompass adenoviruses that were merely contemplated, and thus "known," but not actually made or published. Due to the uncertainty in what recombinant adenoviruses were "known" as contemplated by the definition provided in the specification for "overexpression," the rejection is affirmed.

3. Rejection under 35 U.S.C. § 102(e)

Claims 11-13, 32-44, 60, 61, 68, 69, 72-75, 97-99 and 101-108 stand rejected under 35 U.S.C. § 102(e) as being anticipated by either Henderson or Little.

Appellants appear to group the claims into two groups, with Group I consisting of claims 11-13, 32-44, 101-106 and 108, see Appeal Brief, page 14, and Group II consisting of claims 60, 61, 68, 69, 72-75, 97-99 and 107, see id. at 23. We thus focus on claim 13 as representative of Group I, and claim 60 as representative of Group II.

The examiner first notes that the disclosures of Henderson and Little are very similar, especially as they describe "adenovirus vectors (Ad5), which replicate in neoplastic cells, and their use in treating neoplastic tissue or cells in vivo, e.g. treatment of neoplastic tissue or cancer." Examiner's Answer, page 8. The adenovirus vectors disclosed by the references "comprise tissue or tumor

specific promoters operably linked to one or more adenoviral genes, such as ADP, E1A or E1B." Id.

Henderson and Little also teach embodiments wherein ADP is retained, and that it may be retained within an E3 region, or may be inserted into another adenoviral region, such as A4. See id. at 9. The references also teach that ADP may alternatively be placed under control of a second tissue specific promoter or a heterologous viral promoter, and Little teaches that multiple copies of the ADP coding sequence may be used.

Henderson and Little are also cited for describing

> plasmids for introduction into replication-restricted adenovirus vectors of an E3 region deleted for all E3 coding sequences except for ADP, both with and without the E3 Y leader (Figs. 5A & 5B in both, Example 4 in '293; Example 5 in '862). Both (Example 6) describe a replication-competent adenovirus vector, CN751, comprising such an E3 region (with the Y leader). CN751 is wild type outside the E3 region (otherwise identical to CN702), and is very similar to GZ1. CN571 kills cells more efficiently and releases 10-40 times more virus at 48-72 hours post-infection as compared to a replication competent adenovirus lacking ADP. . . .
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> * * *
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> With respect to claims dependent from claim 13, absent evidence to the contrary, placing ADP expression under control of a heterologous promoter (tissue specific or viral promoters) or inclusion of multiple copies of ADP would be expected to result in overexpression compared to dl309, at least at times early after infection when dl309 expresses little ADP. Claim 60 does not require overexpression of ADP.

Id. at 9-10.

We recognize that in order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44

USPQ2d 1429, 1432 (Fed. Cir. 1997). We find, however, that Henderson and Little teach the invention of representative claims 13 and 60 and thus the rejection is affirmed.

Appellants argue that claims 11-12, 32-44, 101-106 and 108 require overexpression of ADP.[6] Appellants assert that while the examiner has placed the burden on appellants to demonstrate that the vectors of Henderson and Little do not overexpress ADP, it is the Examiner's burden to demonstrate that each and every element of the claims is either explicitly or necessarily disclosed in the prior art reference. See Appeal Brief, page 14.

Moreover, appellants assert, even if the burden was properly shifted, Appellants have demonstrated that the prior art does not teach a vector that overexpresses ADP. Appeal Brief, page 15. Appellants contend that "[b]oth Henderson and Little teach that CN751 expresses about the same amount of ADP as does wild-type adenovirus, and thus cannot be said to overexpress ADP." Id. And as the claims require overexpression relative to *dl*309, and as *dl*309 according to appellants expresses "wild-type" levels of ADP, appellants urge that the CN751 vector taught by Henderson and Little cannot anticipate the claims. See id.

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[6] Appellants do not provide similar arguments that Little and Henderson do not teach the methods of claims 60, 61, 68, 69, 72-75, 97-99, but only argue that Little and Henderson are not available as prior art. See Appeal Brief, page 23. Thus, appellants apparently concede that Little and Henderson anticipate those claims.

Appellents' arguments are not found to be convincing. Claim 13 recites that the "adenovirus vector . . . overexpresses an adenovirus death protein, wherein overexpression is defined as overexpression relative to dl309." The claim does not require any particular level of overexpression, thus all that is required by claim 13 is any measurable level of ADP expression over that of *dl*309.

There is also enough evidence on the record demonstrating that such a level of overexpression would be inherent in the recombinant adenoviruses expressing ADP taught by Henderson and Little, thus the burden has been properly shifted to appellants to demonstrate that the adenoviruses of Little and Henderson do not meet that limitation. See In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) (noting the PTO can require an applicant to establish that a prior art product does not necessarily possess the characteristics of the claimed product when the prior art and claimed products are identical or substantially identical). Appellants prepare the adenoviruses required by the method of claim 13 by deleting the E3 region, and inserting the ADP gene from Ad5. See Specification, Example 1, page 20-21. Similarly, Henderson and Little also deleted the E3 region, and then inserted the ADP gene from Ad2. See Henderson, Col. 48, Example 6, lines 15-33; Little, Col. 38, Example 5, lines 20-25. As the adenoviruses taught by the Henderson and Little and those taught by the instant specification were constructed in an analogous manner, i.e., deletion of the E3 region followed by introduction of an ADP coding

region, absent evidence to the contrary, one of ordinary skill in the art would expect the recombinant adenoviruses of Henderson and Little to express comparable amounts of ADP as the recombinant adenoviruses taught by the instant specification.

Moreover, appellants statement that "[b]oth Henderson and Little teach that CN751 expresses about the same amount of ADP as does wild-type adenovirus, and thus cannot be said to overexpress ADP," is based on the showing in Henderson that Henderson's ADP expressing adenovirus, CN751, "kills cells more efficiently than an ADP-minus control, but about the same as an ADP-positive wild-type control, Rec700," Appeal Brief, page 15, and on the assumption that "cell killing is a good measure of ADP expression," id. (citing Example 2 of the instant specification). Appellents' arguments, however, are based on the assumption that cell killing is directly and always correlated to ADP overexpression. Moreover, as noted above, any increase in expression of ADP over that of *dl*309 would meet the limitation of requiring overexpression of ADP relative to *dl*309, and there is nothing on the record that demonstrates that the recombinant ADP expressing adenoviruses of Henderson and Little do not meet that level of ADP expression. Finally, arguments of counsel cannot take the place of evidence in the record. See in re Scarbrough, 500 F.2d 560, 566, 182 USPQ 298, 302 (CCPA 1974); In re DeBlauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984).

Finally, appellants argue that the present inventors conceived of vectors that overexpress ADP, as well as their use in cancer therapy, before the priority date of the Henderson and Little patents, and were diligent in reducing the invention to practice. See Appeal Brief, pages 16 and 23. Appellants have submitted and rely on two separate declarations filed under 37 CFR § 1.131 to support that assertion.

A Rule 131 declaration, however, cannot be relied on to overcome a reference that claims the same subject matter. See MPEP § 715.05 ("When the reference in question is a noncommonly owned U.S. patent or patent application publication claiming the same invention as applicant and its publication date is less than 1 year prior to the presentation of claims to that invention in the application being examined, applicant's remedy, if any, must be by way of 37 CFR 1.608 instead of 37 CFR 1.131."). See also MPEP § 2308.

For example, claim 13 is drawn to a method for treating cancer in an animal having a tumor wherein the adenovirus overexpresses ADP relative to *dl*309. Claim 63 of the Little patent is drawn to a method of suppressing tumor cell growth in an individual having an AFP-expressing tumor by administering an adenovirus vector comprising a sequence encoding ADP, wherein E1A and E1B of the adenovirus vector are under transcriptional control of α-fetoprotein transcription regulatory elements. Thus, representative claim 13 is generic to Little's claim 63. Similarly, claim 60 of the claims on appeal encompasses a method for treating cancer in an animal having a tumor, wherein an adenovirus

vector that is replication competent and expresses ADP is administered to the tumor, wherein the ADP is expressed from an ADP coding sequence other than the endogenous promoters for ADP. Thus, representative claim 60 is also generic to Little's claim 63.

Instead, Appellants must make the showing required by 37 CFR § 41.202 in order to provoke an interference with the Henderson/Little patents.[7] Rule 202 reads as follows:

> § 41.202 Suggesting an interference
>
> (a) Applicant. An applicant, including a reissue applicant, may suggest an interference with another application or a patent. The suggestion must:
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> (1) Provide sufficient information to identify the application or patent with which the applicant seeks an interference,
>
> (2) Identify all claims the applicant believes interfere, propose one or more counts, and show how the claims correspond to one or more counts,
>
> (3) For each count, provide a claim chart comparing at least one claim of each party corresponding to the count and show why the claims interfere within the meaning of § 41.203(a),
>
> (4) Explain in detail why the applicant will prevail on priority,
>
> (5) If a claim has been added or amended to provoke an interference, provide a claim chart showing the written description for each claim in the applicant's specification, and
>
> (6) For each constructive reduction to practice for which the applicant wishes to be accorded benefit, provide a chart showing where the disclosure provides a constructive reduction to practice within the scope of the interfering subject matter.
>
> . . .

[7] 37 CFR § 1.608 was replaced by 37 CFR § 41.202, effective September 2004. The new rule will control future proceedings in this case.

> (d) Requirement to show priority under 35 U.S.C. § 102(g). (1) When an applicant has an earliest constructive reduction to practice that is later than the apparent earliest constructive reduction to practice for a patent or published application claiming interfering subject matter, the applicant must show why it would prevail on priority.
>
> (2) If an applicant fails to show priority under paragraph (d)(1) of this section, an administrative patent judge may nevertheless declare an interference to place the applicant under an order to show cause why judgment should not be entered against the applicant on priority. New evidence in support of priority will not be admitted except on a showing of good cause. The Board may authorize the filing of motions to redefine the interfering subject matter or to change the benefit accorded to the parties.
>
> (e) Sufficiency of showing. (1) A showing of priority under this section is not sufficient unless it would, if unrebutted, support a determination of priority in favor of the party making the showing.

4. Rejection under 35 U.S.C. § 103(a)

Claims 13, 20-22, 60 and 64-66 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Henderson or Little as combined with Freytag.

Henderson and Little are relied upon as above. Freytag is cited for teaching "a novel three-pronged approach to kill cancer cells selectively comprising administration of a cytolytic replication-competent, E1B-atenuated adenovirus in conjunction with chemotherapy . . . and radiation." Examiner's Answer, pages 10-11. The Answer concludes:

> At the time the invention was made it would have been obvious for one of ordinary skill in the art to combine the chemotherapy/radiation combination approach of Freytag when using the replication-competent adenovirus vectors of Henderson or Little, since Freytag teaches the enhanced cell killing properties

> when using a three-pronged approach involving additional modalities, combining a replication-competent adenovirus in conjunction with chemotherapy and radiation. Thus the invention was prima facie obvious at the time the invention was made.

Id. at 11.

The burden is on the examiner to set forth a prima facie case of obviousness. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988). We find that the examiner has met that burden, and the rejection is affirmed.

Appellants first argue that Henderson and Little are not available as prior art, and Freytag alone does not teach or suggest the claimed invention. See Appeal Brief, page 25. As noted above, a Rule 131 declaration, however, cannot be relied on to overcome a reference that claims the same subject matter, and thus Henderson and Little are available as prior art.

Appellants argue further with respect to claims 13 and 60 that "Freytag adds nothing to the teachings of Henderson and Little that is relevant to the subject matter of these claims." Id. at 26. With respect to the dependent claims, appellants contend that there is no mention of the ADP gene, nor of vectors employing the ADP gene, thus the reference provides no motivation to employ radiation "except in connection with vectors that bear the special suicide CD/HSV-1 TK gene construct." Id. at 27.

Obviousness is determined in view of the sum of all of the relevant teachings in the art, not isolated teachings in the art. See In re Kuderna,

426 F.2d 385, 389, 165 USPQ 575, 578 (CCPA 1970); see also In re Shuman, 361 F.2d 1008, 1012, 150 USPQ 54, 57 (CCPA 1966). Appellants are focusing on Freytag in isolation and are not considering its teachings in view of the prior art as a whole.

As noted by the rejection, Freytag teaches "a novel three-pronged approach to kill cancer cells selectively comprising administration of a cytolytic replication-competent, E1B-atenuated adenovirus in conjunction with chemotherapy . . . and radiation." Thus, it would have been obvious for one of ordinary skill in the art to combine the chemotherapy/radiation combination approach of Freytag when using the replication-competent adenovirus vectors of Henderson or Little, since Freytag teaches the enhanced cell killing properties when using a three-pronged approach involving additional modalities, combining a replication-competent adenovirus in conjunction with chemotherapy and radiation, and the rejection is affirmed.

CONCLUSION

The rejection of claims 11-15, 20-22, 24, 33-44, 60-75 and 97-102, 107 and 108 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, i.e., new matter, is reversed, but the rejection is affirmed as to claims 32 and 104-106. The rejection of 101 and 102 under 35 U.S.C. §112, second paragraph, as being indefinite, however, is affirmed. The rejection of claims 11-13, 32-44, 60, 61, 68, 69, 72-75, 97-99 and 101-108 under 35 U.S.C. §102(e) as being anticipated by either Henderson or Little is

affirmed. Moreover, we have not considered the declarations filed under 37 CFR 131 as a Rule 131 declaration cannot be relied on to overcome a reference that claims the same subject matter. We also affirm the rejection of claims 13, 20-22, 60 and 64-66 under 35 U.S.C. § 103(a) as being unpatentable over Henderson or Little as combined with Freytag.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Joan Ellis)
Administrative Patent Judge)
)
)
) BOARD OF PATENT
Donald E. Adams)
Administrative Patent Judge) APPEALS AND
)
) INTERFERENCES
)
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